Remarks

Claim 92 is pending in this application. Pursuant to restriction requirement and election of species, claims 61-63, 67-91, and 93-94 are canceled without prejudice to Applicants' right to pursue the subject matter recited by them in one or more divisional, continuation, and continuation-in-part applications. No new matter has been introduced.

Applicants respectfully submit that claim 92 is allowable for at lest the following reasons.

A. Obviousness-Type Double Patenting Rejections

Claim 92 has been rejected under the judicially created doctrine of obviousness-type double patenting over claims 4 and 10-15 of U.S. Patent No. 6,911,479 ("the '479 patent"). Applicants respectfully submit that claims 4 and 10-15 of the '479 patent recite limitations that render those claims patentably distinct from the claims pending in this application. Nevertheless, without acquiescing to this rejection, Applicants submit herewith a terminal disclaimer over the '479 patent to expedite the prosecution of the present application. In view of this terminal disclaimer, Applicants respectfully request that this rejection be withdrawn.

Claim 92 has also been rejected under the judicially created doctrine of obviousness-type double patenting over claims 1, 4, 12, 14-16, and 61 of U.S. appl. no. 11/091,518 ("the '518 application")[1]. Specifically, it is alleged that the claims in this application and in the '518 application "are not patentably distinct from each other because they both are directed to methods of treating anxiety comprising administering to a patient a salt of (-)-O-desmethylvenlafaxine." (Office Action, pages 3-4). Applicants must respectfully disagree for at least the following reason: the claims currently pending in the '518 application do not recite any method of treatment or a method of treating anxiety. A copy of the most current claims in the '518 application, which were submitted with Applicants' response dated May 5, 2008, is attached hereto as Exhibit A. As the Examiner will see, all of the claims pending in the '518 application recite pharmaceutical compositions of racemic ODMV succinate. Thus, Applicants respectfully request that this rejection be withdrawn.

[1] The Office Action indicates the application no. to be 11/091,581. However, Applicants believe that the Office Action meant to refer to application no. is presumably 11/091,518, and Applicants respond here on that basis.

B. The Rejection Under 35 U.S.C. §103

On pages 5-7 of the Office Action, claim 92 is rejected as allegedly obvious over EP 0639374 A2 to Rudolph *et al.* ("the '374 publication"). The Office Action acknowledges that the '374 publication "does not explicitly teach a method of treating anxiety with the (-)-enantiomer of O-desmethylvenlafaxine," but alleges that claim 92 would have been obvious because "the skilled artisan would have expected optical isomers to be separable and isomers so separated to exhibit physiological effects at varying levels." (Office Action, page 6). The Office Action also alleges that "[i]t is well-settled [in] patent law that optical isomers would have been expected to possess different therapeutic activities. (*Id.* at page 7). Applicants respectfully disagree with each of these allegations.

It is Applicants' understanding that the Office Action's basis for rejection essentially amounts to the proposition that no claims to optical isomers are *prima facie* non-obvious over prior disclosure of racemic mixture. Applicants must respectfully point out, however, that such a proposition is contrary to the well-settled principles in patent law regarding the *prima facie* case of obviousness.

Prior decisions of courts, including the Court of Appeals for the Federal Circuit ("Federal Circuit"), as well as of the Board of Patent Appeals and Interferences ("BPAI") clearly support the proposition that fairly specific suggestion for a claimed single isomer (or the uses thereof), or at least a reasonable expectation of successfully making and using such a single isomer, is essential in establishing a *prima facie* case of obviousness.

The Office Action's obviousness contention appears to fail to take into consideration that, in 2007, following the Supreme Court's landmark ruling in *KSR*, the Federal Circuit affirmed the patentability of chiral pharmaceutical compounds. (*See Forest Labs., Inc. v. Ivax Pharmaceuticals, Inc.*, 501 F.3d 1263 (Fed. Cir. 2007), *aff'g* 438 F.Supp.2d 479 (D. Del. 2006)). Similar to the issue in the instant application, *Forest* specifically addressed the issue of whether a single enantiomer of a pharmaceutical compound can be nonobvious and patentable in view of a prior art disclosure of the pharmaceutical compound's racemate. (*See id.* at 492-96). The Federal Circuit ruled that claims to the single enantiomer pharmaceutical compound were valid and nonobvious. (*See id.*).

In reaching this holding, the Federal Circuit in *Forest* affirmed the "district court's key factual findings underlying its conclusions on obviousness," which are of particular relevance to the obviousness rejection in the instant application. In particular, the District Court determined that the "unpredictable nature of the separation of racemic compounds" meant that "a person skilled in the art seeking such a resolution *would not*

have a reasonable expectation of success without undue experimentation." (*See Forest*, 438 F.Supp.2d at 493 (emphasis added); *see also Forest*, 501 F.3d at 1269 ("[T]he district court's key factual findings underlying its conclusions on obviousness are not clearly erroneous.")). In fact, following *KSR*, the Federal Circuit has repeatedly stressed that obviousness determinations in the pharmaceutical arts must involve an assessment of whether a skilled artisan would have possessed a reasonable expectation of success. (*See Forest*, 501 F.3d at 1269; *Takeda Chemical Industries, Ltd. v. Alphapharm Pty. Ltd.*, 492 F.3d 1350, 1360-62 (Fed. Cir. 2007) (finding claimed pharmaceutical compound nonobvious because, inter alia, there existed "no reasonable expectation [of success] in the art.")).

Following Federal Circuit precedent, a U.S. District Court recently upheld the patentability of a single enantiomer drug in view of the prior art disclosure of its racemate. (*See Sanofi-Synthelabo v. Apotex, Inc.*, 492 F.Supp.2d 353, 390 (S.D.N.Y 2007)). Again stressing the importance of determining whether a skilled artisan would have possessed a reasonable expectation of success, the Court concluded that the claimed enantiomer was nonobvious because, *inter alia*, "the prior art did not enable a person of ordinary skill in the art to predict with a reasonable expectation of success whether one enantiomer of [the claimed compound] would have better pharmaceutical properties than the racemate itself . . . .") (emphasis added)).

Therefore, allegations that claims to a single enantiomer are *per se prima facie* obvious over prior disclosure of racemic mixture are directly contrary to numerous court decisions discussed above. Further, to the extent that the Examiner is relying on the proposition that "optical isomers would have been expected to possess different therapeutic activities," Applicants respectfully point out that such a proposition, even if taken as true, would not be sufficient to satisfy the reasonable expectation of success as required by the case law. This is because the question to be asked in assessing reasonable expectation of success is not whether one would have expected that optical isomers would possess different therapeutic activities. Rather, the question is whether one would have reasonably expected the claimed optical isomer would be pharmaceutically more advantageous.

In this regard, Applicants respectfully submit that the '374 publication falls far short of providing any expectation of success in connection with Applicants' present claim 92. For example, although anxiety is disclosed in the '374 publication as one of various disorders that may allegedly be treated by racemic ODMV, there is no teaching or suggestion in the '374 publication that would have provided to those skilled in the art with

any expectation of successfully treating the specific disorder anxiety using the specific ODMV enantiomer as recited in Applicants' present claim 92.

In addition, there is no disclosure or guidance in the '374 publication that would enable those skilled in the art to "predict with a reasonable expectation of success whether [the claimed (-)-isomer] would have better pharmaceutical properties than the racemate itself." (*Sanofi-Synthelabo*, 492 F.Supp.2d at 390). Consequently, Applicants respectfully submit that no *prima facie* case of obviousness is established by the '374 publication, and thus, respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

C. Conclusion

For at least the foregoing reasons, Applicants respectfully submit that claim 92 is allowable, and thus, respectfully request the withdrawal of its rejections.

No fee is believed to be due for the submission of this paper. If any fees are required for the submission of this paper, or to avoid abandonment of this application, the Director is authorized to charge the required fees to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

Date June 13, 2008 L0209

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Exhibit A

Amendments to the Claims

The listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (Currently amended) A pharmaceutical composition which comprises (±)-O-desmethylvenlafaxine succinate ~~, or a pharmaceutically acceptable salt, solvate, or clathrate thereof,~~ and a pharmaceutically acceptable carrier or excipient, wherein (±)-O-desmethylvenlafaxine is present at an amount of about 50 mg.

2-11. (Canceled).

12. (Currently amended) The ~~dosage form of claim 11~~ pharmaceutical composition of claim 1, wherein said ~~dosage form~~ composition is in a form of a tablet ~~or a capsule~~.

13-59. (Canceled).

60. (New) The pharmaceutical composition of claim 12, which is a controlled-release formulation.

61. (New) The pharmaceutical composition of claim 12, wherein the tablet is coated.

62. (New) The pharmaceutical composition of claim 1, wherein the carrier or excipient is microcrystalline cellulose, talc, magnesium stearate, sodium carboxycellulose, stearic acid, or a combination thereof.

63. (New) The pharmaceutical composition of claim 1, wherein the composition is adapted for once a day administration.

64. (New) A pharmaceutical composition which comprises (±)-O-desmethylvenlafaxine succinate and a pharmaceutically acceptable carrier or excipient, wherein (±)-O-desmethylvenlafaxine is present at an amount of about 100 mg.

65. (New) The pharmaceutical composition of claim 64, wherein said composition is in a form of a tablet.

66. (New) The pharmaceutical composition of claim 65, which is a controlled-release formulation.

67. (New) The pharmaceutical composition of claim 65, wherein the tablet is coated.

68. (New) The pharmaceutical composition of claim 64, wherein the carrier or excipient is microcrystalline cellulose, talc, magnesium stearate, sodium carboxycellulose, stearic acid, or a combination thereof.

69. (New) The pharmaceutical composition of claim 64, wherein the composition is adapted for once a day administration.